REMARKS

Claims 1-24, which are pending in the present application are canceled herein and replaced with new claims 25-51. Accordingly, new claim 25-51 are presented for examination on the merits.

Applicants and applicants' counsel would like to thank the Examiner for taking the time to conduct an interview concerning the outstanding issues in this case and for the suggested amendments to the claims.

The specification has been amended to include priority information and to clarify the information provided by original Figure 13. Original Figure 13 has been replaced herein with a new Figure 13, which corrects a typographical error in the original drawing that consisted of an inadvertent deletion of a "T" in the nucleotide sequence of OAV287 at position 24805.

The specification and original claims 1-24 support new claims 25-48. The amendments to the specification and claims do not add new matter.

Applicants also enclose a new Declaration.

I. Objections to the Drawings

Applicants request entry of the proposed substitute sheet of drawing filed May 16, 2001. The proposed drawing does not contain new matter and merely corrects a typographical error, resulting from a previous amendment to Figure 1. A detailed

explanation of the way in which the error occurred is provided by way of a declaration under 35 U.S.C. § 1.132 of Dr. Wayne Both, which is enclosed herewith.

It is submitted that replacement of the Figure 13 with a corrected version will eliminate any confusion caused by a typographical error in the original drawing. Replacement of the drawing merely makes explicit that which was implicit in the original drawings.

Accordingly, the objection to the drawing is respectfully traversed.

II. Objections to the Specification

The Examiner objected to the Sequence List provided with the response filed May 16, 2001 because of the presence of a "t" residue at position 24805 and "X's" at various positions within the sequence.

Applicants have amended the specification to clarify the description of Figure 13, which shows the nucleotide sequence of pOAV100, a plasmid containing the BluScript plasmid vector and a modified OAV287 genome (Figure 1 illustrates the "unmodified" OAV287 genome). The modified OAV287 sequence contains an **X** (in bold and larger font than the surrounding letters) between nucleotide residues at two positions in the sequence illustrated in Figure 13, as well as several additional nucleotides inserted throughout the sequence. The additional nucleotides are also offset in bold and are larger than the surrounding letters. The Examiner correctly notes that X's do not

designate a residue in a nucleotide sequence. Indeed, the two X's were inserted in Figure 13 as a means of illustrating differences between the nucleotide sequence shown in Figure 1 and the nucleotide sequence shown in Figure 13. The X's in original Figure 13 merely indicate one type of modification to the OAV287 sequence that is shown in Figure 13, i.e., the absence of a nucleotide which occurs at the corresponding position in the sequence shown in Figure 1. Placement of an X in the figure is merely a means of graphically illustrating a positional difference between the OAV287 sequence of Figure 1 and the modified OAV sequence of Figure 13. It is respectfully submitted that one of skill in the art would readily recognize the meaning of the X's in Figure 13.

Accordingly, the formal grounds of objection to the specification are respectfully traversed. It is respectfully requested that the Sequence List, which was filed May 16, 2001, in both paper and computer readable form, be entered in the present application.

III. Objections to the Claims

It is respectfully submitted that the amendments to the claims render the objections thereto moot.

IV. Rejection of Claims 1, 2, 8-11 and 24 Under 35 USC § 112, First Paragraph

The Examiner acknowledges that the specification is enabling for isolated DNA sequences comprising a nucleotide sequence identical to all or part of SEQ ID NO. 1 or of Figure 13 (which sets forth SEQ ID NO. 3) and variants of these sequences comprising differences in the viral protein coding sequences that do not alter the amino acid sequence encoded thereby. However, the Examiner states that the specification does not provide enablement for nucleotide sequence that encode other variants of these sequences.

This rejection is respectfully traversed as follows.

Applicants agree with the Examiner that the specification provides an enabling description of the nucleotide sequences set forth in the Sequence List and Figure13, as well as variants thereof that contain silent mutations in coding regions of the genome. However, the specification also discloses several nucleotide modifications to the sequences that alter noncoding regions of the sequences, as well as modifications that alter the protein sequence, e.g., loss of the SalI site in two major open reading frames, which does not effect virus infectivity or replication.

Moreover, the present claims require that the DNA molecule has the nucleotide sequence of SEQ ID NO. 3 (nucleotides 1-29,574) or specifically hybridizes the complement thereof under high stringency conditions, and comprises the ovine adenovirus genome. One of ordinary skill in the art would not expect much variation among species of DNA molecules encompassed by the claims because the

hybridization conditions set forth in the claims yield structurally similar DNAs, all of which encode a functional ovine adenovirus genome.

Accordingly, the rejection of claims 1, 2, 8-11 and 24 under 35 USC § 112, first paragraph is respectfully traversed.

V. Rejection of Claims 4-7 Under 35 USC § 112, First Paragraph

It is respectfully submitted that the amendment to the claims render the rejection of claims 4-7 moot.

VI. Rejection of Claims 3, 12-17, 21 and 22 Under 35 USC § 112, First Paragraph

The Examiner states that the specification does not enable one of skill in the art to make and use DNA molecules or vectors as set forth in original claims 3, 12-17, 21 and 22 that encode altered polypeptide or contain less than the whole genome of OAV287 as shown in SEQ ID NO. 1.

Applicants respectfully disagree with the Examiner's conclusion.

New claims 29, 50 and 51, which correspond to original claims 3, 14 and 17 are directed to DNA molecules, plasmids and vectors, respectively, that contain an alteration or deletion in an area of the OAV287 genome shown in the specification to be non-essential for viral replication and maintenance of viable virus. At page 20 of the specification, a plasmid in which the open reading frames defined by the sequence

spanning nucleotides 28457-29014 and nucleotides 28511- 28699 was disrupted is described (pOAV600S). Despite the disruption of the two open reading frames viable virus was obtained from cells transfected with the plasmid, illustrating unequivocally that these two regions of the OAV287 genome are non-essential for virus viability. Thus, the invention claimed in claims 29, 30, 50 and 51 meets the requirements of 35 USC § 112, first paragraph.

New claims 36-41, 45 and 46 which correspond to original claims 12-17, are directed to viral vectors comprising a nucleic acid molecule having a specified nucleotide sequence or which hybridize under high stringency conditions to a specified nucleotide sequence and which functions as an ovine adenovirus genome. The specification discloses that viable ovine adenovirus is obtained after transfection of cells with the viral vectors set forth in these claims (See page 22, lines 8-14) and heterologous genes encoded by the vectors are expressed in transfected cells (See page 23, lines 10-20 and Figure 12A). Thus, the claims satisfy the requirements of 35 USC § 112, first paragraph.

Accordingly, the rejection of claims 3, 12-17, 21 and 22 under 35 USC § 112, first paragraph is respectfully traversed.

VII. Rejection of Claims 18-20 and 23 Under 35 USC § 112, First Paragraph

The Examiner states that the lack of working examples in the specification, coupled to the high unpredictability in the art of *in vivo* DNA transfer with respect to gene therapy and genetic engineering uses and the unpredictable problems associated with use of new vectors would require undue experimentation to practice the claimed invention *in vivo*.

Applicants respectfully disagree with the Examiner's assertions.

The Examiner has made an unfounded assertion that the claimed invention requires therapeutic effect. However, claims 42, 43, 44 and 47 do not set forth such limitations and specifically do not require therapeutic effect. The claims merely require that a viral vector of the invention encoding a non-adenovirus polypeptide transfect at least one cell of the animal to which they are administered and express the non-adenovirus gene in the transfected cell(s).

The specification provides a working example of the invention set forth in claims 42-44 and 47 at page 23, lines 21-28. It is disclosed that a recombinant virus of the invention was administered to sheep intraconjunctivally, as well as intranasally. At three days post inoculation recombinant virus was recovered from a nasal swab of one sheep and from conjunctival swabs of two other sheep. The identity of the obtained virus was proved by PCR analysis.

The specification also discloses that expression of the foreign gene is obtained. Figures 11 and 12 demonstrate that the OAV287 vector of the invention successfully expresses foreign genes inserted therein when used to infect host cells. As such, the specification provides an enabling disclosure of the invention set forth in claims 42-44 and 47.

Accordingly, the rejection of claims 18-20 and 23 (now claims 42-44 and 47) under 35 USC § 112, first paragraph is respectfully traversed.

VIII. Rejection of Claims 1-23 Under 35 USC § 112, Second Paragraph

It is respectfully submitted that the rejection to claims 1-23 is rendered moot by the amendment to the claims.

It is respectfully submitted that the present application, as amended is in condition for allowance, an early notification thereof being earnestly solicited. The Examiner is invited to contact Applicants' representative at the telephone number listed below if there are any questions or issues requiring clarification.

Please charge any additional fees or credit any overpayment in connection with this communication to Deposit Account 50-0417.

Respectfully submitted,

McDERMOTT, WILL & EMERY

Date: July 10, 2002

By: 

Judith L. Toffenetti
Registration No. 36,139

600 13th Street, N.W., Suite 1200
Washington, D.C. 20005-3096
Telephone: 202-756-8000
Facsimile: 202-756-8087

VERSION WITH MARKINGS TO SHOW CHANGES MADE

On page 1 of the specification following the title please replace the first paragraph with the following.

--This application is a Continuation Application of parent application, Serial No.09/464,767, which is a Continuation-In-Part Application of Serial No. 08/776,274, filed January 24, 1997, (abandoned) as the National Phase of PCT Application No. PCT/AU95/00453, filed July 26, 1995 and claiming priority to Australian Application No. PM7101, filed July 26, 1994.--

Please replace the paragraph after line 27 of page 8 as amended in the Preliminary Amendment of May 16, 2001 with the following:

--Figure 13 is [a modified nucleic acid sequence of the OAV287 genome beginning at base 1 of the left hand ITR] the nucleotide sequence of a plasmid containing a modified OAV287 genome which begins at base 1 of the left hand ITR and continues through to the end of the OAV287 sequence (29,574). (SEQ ID NO. 3). The positions of changes in the sequence (in comparison to the sequence illustrated in Figure 1) are indicated by bold letters offset in larger font than the surrounding letters; actual nucleotide additions to the sequence are indicated by a letter representing a nucleotide (A,G,C or T) and the deletion of a nucleotide from the corresponding

sequence set forth in Figure 1 is indicated by an X (in bold and of larger font). Nucleotides 1-29,574 represent OAV287 sequence; nucleotides 29,575-32,7454 represent Bluescribe plasmid sequence.--

Please replace the paragraph on page 10, after line 15, as amended in the Preliminary Amendment of May 16, 2001 with the following:

--When used herein "high stringency" refers to conditions that:

(i) employ low ionic strength and high temperature for washing after hybridization, for example, 0.1 X SSC and 0.1% (w/v) SDS at 50° C; and

(ii) employ during hybridization conditions such that the hybridization temperature is [250°] 25°C lower than the duplex melting temperature of the hybridizing polynucleotides, for example 1.5 X SSPE, 10% (w/v) polyethylene glycol 6000 (Amasino, 1986), 7% (w/v) SDS (Church, 1984), 0.25 mg/ml fragmented herring sperm DNA at 65° C; or [(iii)] for example, 0.5 M sodium phosphate, pH 7.2. 5mM EDTA, 7% (w/v) SDS (Church, 1984) and 0.5% (w/v) BLOTTO (Johnson, 1984; Reed, 1985) at 70° C; or

[(iv)] (iii) employ during hybridization a denaturing agent such as formamide (Casey, 1977), for example, 50% (w/v) formamide with 5 X SSC, 50 mM sodium phosphate (pH 6.5) and 5 X Denhardt's solution (Denhardt, 1996) at 42°C; or [(v)]

employ, for example, 50% (w/v) formamide, 5 X SSC, 50 mM sodium phosphate (pH6.8), 0.1% (w/v) sodium pyrophosphate,5 X SSC Denhardt's solution (Denhardt, 1996), sonicated salmon sperm DNA [(50 5g/ml)] (50 µg/ml) and 10% dextran sulphate (Wahl, 1979) at 42°C. See generally references Meinkoth, 1984; Reed, 1991; Dyson, 1991.--

Please cancel claims 1-24 and replace them with new claims 25-48 as follows:

Claim 25. An isolated DNA molecule comprising nucleotides 1-29,574 of SEQ ID NO. 3 or an isolated DNA molecule that hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency conditions and which encodes a functional ovine adenovirus genome.

Claim 26. The isolated DNA molecule of claim 1 wherein the DNA molecule specifically hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 13 and shares at least 90% identity therewith.

Claim 27. The isolated DNA molecule of claim 25 wherein the nucleotide sequence is a variant of nucleotide 1-29,574 of SEQ ID NO. 3 which comprises at least one nucleotide difference in the ovine adenovirus genomic sequence that does not alter the amino acid sequences encoded thereby.

Claim 28. An isolated DNA molecule comprising the OAV287 inverted terminal repeat consisting of nucleotides 1 through 46 of SEQ ID NO. 3.

Claim 29. An isolated DNA molecule having a nucleotide sequence which specifically hybridizes under high stringency conditions to the complement nucleotide 1-29,574 of SEQ ID NO. 3, wherein the DNA molecule comprises an ovine adenovirus genome from which all or part of a nonessential portion encoding genetic information that is not essential to the maintenance or viability of the ovine adenovirus has been deleted or altered, said nonessential portion comprising an open reading frame comprising nucleotides 28457 through nucleotide 29014 of the complement of SEQ ID NO. 3 or an open reading frame comprising nucleotides 28511 through nucleotide 28699 of the complement of SEQ ID NO. 3.

Claim 30. A plasmid having the structure of pOAV600 or pOAV200.

Claim 31. A plasmid comprising a bacterial origin of replication and a first nucleotide sequence as set forth in nucleotides 1-29,574 of SEQ ID NO. 3 or a second nucleotide sequence that specifically hybridizes to the complement of nucleotides 1-

29,574 of SEQ ID NO. 3 under high stringency conditions and which comprises a functional ovine adenovirus genome.

Claim 32. The plasmid of claim 31 wherein the second nucleotide sequence hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 and shares at least 90% identity therewith.

Claim 33. The plasmid of claim 31 or 32 wherein the first or second nucleotide sequence is operatively linked to a third nucleotide sequence encoding a non-adenovirus polypeptide.

Claim 34. The plasmid of claim 33 wherein the inverted terminal repeats of the first nucleotide sequence are linked together or the inverted terminal repeats of the second nucleotide sequence are linked together.

Claim 35. The plasmid of claim 33 or 34 wherein the third nucleotide sequence encodes resistance to an antimicrobial agent.

Claim 36. A vector comprising (1) a first nucleotide sequence having the sequence as set forth in nucleotides 1-29,574 of SEQ ID NO. 3 or a second nucleotide

sequence that specifically hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency conditions and which comprises the ovine adenovirus genome; and (2) a third nucleotide sequence encoding at least one non-adenoviral polypeptide operatively linked to the first or second nucleotide sequence.

Claim 37. The vector of claim 36 wherein the second nucleotide sequence specifically hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 and shares at least 90% identity therewith.

Claim 38. The vector of claim 37 comprising the second nucleotide sequence operatively linked to a third nucleotide sequence encoding at least one non-adenoviral polypeptide.

Claim 39. The vector of any one of claims 36-38 wherein the non-adenoviral polypeptide is a bacterial, viral, parasite or eucaryotic polypeptide.

Claim 40. The vector of claim 39 wherein the non-adenoviral polypeptide is selected from rotavirus VP7sc antigen, *Trichostrongylus colubriformis* 17 kD antigen, *Taenia ovis* 45W antigen and *Lucila cuprina* PM95 antigen.

Claim 41. A method of delivering a DNA molecule encoding at least one non-adenoviral polypeptide to a target cell comprising transfecting the target cell with a vector comprising (1) a first nucleotide sequence set forth in nucleotides 1-29,574 of SEQ ID NO. 3 or a second nucleotide sequence that hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency conditions and which comprises the ovine adenovirus genome; and (2) a third nucleotide sequence encoding at least one non-adenoviral polypeptide, wherein the at least one polypeptide is expressed in the target cell.

Claim 42. A method of delivering a DNA molecule encoding at least one non-adenoviral polypeptide to an animal comprising administering to the animal a vector comprising (1) a first nucleotide sequence as set forth in nucleotides 1-29,574 of SEQ ID NO. 3 or a second nucleotide sequence that specifically hybridizes to the complement of nucleotide 1-29,574 of SEQ ID NO. 3 under high stringency conditions and which comprises the ovine adenovirus genome; and (2) a third nucleotide sequence encoding at least one non-adenoviral polypeptide,
wherein the vector tranfects at least one cell of the animal and the at least one polypeptide is expressed therein.

Claim 43. The method of claim 42 wherein the vector is administered to a grazing animal.

Claim 44. The method of claim 43 wherein the vector is administered to a sheep.

Claim 45. A vector comprising (1) a first nucleotide as set forth in SEQ ID NO. 3 or a second nucleotide sequence that specifically hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency conditions and which comprises the ovine adenovirus genome; and (2) a nucleotide sequence encoding an RNA molecule.

Claim 46. The vector of claim 45 wherein the RNA molecule is an antisense RNA molecule or ribozyme.

Claim 47. A method of delivering a DNA molecule encoding a functional RNA molecule to an animal comprising administering to the animal a viral vector comprising (1) a first nucleotide sequence as set forth in SEQ ID NO. 3 or a second nucleotide sequence that specifically hybridizes to the complement of nucleotides 1-29,574 of SEQ ID NO. 3 under high stringency conditions and which comprises the ovine adenovirus genome; and (2) a nucleotide sequence encoding an RNA molecule, wherein the vector

transfects at least one cell of the animal and the nucleotide sequence encoding the RNA molecule is expressed therein.

Claim 48. A plasmid comprising a DNA molecule having the nucleotide sequence as set forth in SEQ ID NO. 3.

Claim 49. A plasmid comprising a DNA molecule having a first nucleotide sequence that specifically hybridizes to nucleotides 1-29574 of SEQ ID NO. 3 under high stringency conditions and which comprises the ovine adenovirus genome operatively linked to a second nucleotide sequence encoding a bacterial origin of replication, wherein the first nucleotide sequence comprises ovine adenovirus inverted terminal repeat sequences that are linked by a third nucleotide sequence which contains at least one unique restriction enzyme site that is not present in the ovine adenovirus genome.

Claim 50. A plasmid comprising the DNA molecule of claim 29.

Claim 51. A vector comprising the DNA molecule of claim 29.